compared with those using the diaphragm when they refer to these two conditions occurring among users of the oral contraceptive?

I would be grateful if this point could be clarified as the text does not do so.

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*. *We sent a copy of this letter to Dr Mann, whose reply is printed below.—Ed, *BMJ*.

SIR,—Table II in our paper certainly does refer to excess mortality attributable to oral contraceptives. This is clearly stated in the last line of the table but I do accept that it might have been helpful to have made this point clear also in the table heading.

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Diagnosis of brain death

SIR,—While we welcome wholeheartedly the clarification provided by the statement concerning the diagnosis of brain death issued by the Conference of Medical Royal Colleges and their Faculties in the United Kingdom (13 November, p 1187) we feel that it is unfortunate that the two references to electroencephalographic technique are incorrectly cited. They should read: "International Federation of EEG Societies. *Electroencephalography and Clinical Neurophysiology*, 1974, 37, 530; 1970, 28, 536."

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Additives to intravenous fluids

SIR,—We were interested to read in your leading article on this subject (31 July, p 264) that "continuous intravenous infusion is indicated only for antibiotics which are too toxic or irritant to be given intermittently—for example, tetracyclines and fusidic acid." We should like to report the successful use of a rapid intermittent intravenous infusion of diethanolamine fusidate with cloxacillin in a boy with staphylococcal osteomyelitis and septicaemia.

A 7-year-old boy presented with a 24-h history of pain since being kicked on the left ischium. Examination revealed a sick, limping child with a temperature of 38.2°C. The soft tissue over the left ischium was tender, but passive movement of both hips was possible. A clinical diagnosis of osteomyelitis was confirmed by blood culture taken on admission, which grew a *Staphylococcus aureus* resistant to benzylpenicillin, ampicillin, tetracycline, and neomycin but sensitive to methicillin, cloxacillin, chloramphenicol, erythromycin, trimethoprim, clindamycin, sodium fusidate, and gentamicin.

The following day the ischium became exquisitely tender, the temperature rose to 39°C, and the peripheral white cell count was $29 \times 10^9/l$ ($29\,000/mm^3$), 88% of which were neutrophils. Intravenous benzylpenicillin (0.5 g four-hourly) and cloxacillin (0.5 g four-hourly) were given in dextrose saline. Four blood cultures taken during the first two days after admission grew *Staph aureus* with the same antibiotic sensitivity pattern.

Two days later, after two operations which had shown no pus formation, the child developed a paralytic ileus and anuria. A rapid intravenous infusion of diethanolamine fusidate (290 mg, equivalent to 250 mg of sodium fusidate) in dextrose saline (540 ml) was then given over 15 min every four hours, the benzylpenicillin being withdrawn but the cloxacillin injections continued. Within 24 h the patient was afebrile and subsequently made an uneventful recovery. Intermittent intravenous infusions of diethanolamine fusidate with cloxacillin were continued for four days and he took oral flucloxacillin (0.5 g) with sodium fusidate (250 mg) four times a day for several months after discharge.

As one possible cause for the failure of this patient to respond to intravenous cloxacillin was its inactivation in the dextrose saline infusion¹ the antibiotic activity was measured after mixing cloxacillin (0.5 g) with normal saline, dextrose saline, and 5% dextrose infusions (540 ml). There was no loss of antibacterial activity during the six hours for which these infusions were left at room temperature.

It is noteworthy that, although cloxacillin was ineffective, the combination of diethanolamine fusidate with cloxacillin rapidly cured this child's staphylococcal septicaemia. The history illustrates the value of rapid intermittent intravenous infusions of diethanolamine fusidate and cloxacillin in staphylococcal osteomyelitis complicated by septicaemia.

In a further study of eight normal subjects a rapid intravenous infusion of diethanolamine fusidate (580 mg, equivalent to 500 mg of sodium fusidate) was given over 15 min. This was well tolerated. Thrombophlebitis² did not follow these infusions in any normal subject or in the child with septicaemia. There was also no evidence of haemolysis.³ Thus in nine subjects intermittent intravenous infusions of diethanolamine fusidate given over 15–20 min were safe and well tolerated. These may be life-saving in acute staphylococcal osteomyelitis and septicaemia.

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¹ Simberhoff, M S, et al, *New England Journal of Medicine*, 1970, 283, 116.

² Copperman, I J, *British Journal of Clinical Practice*, 1972, 26, 83.

³ Manufacturers' literature.

New enterotoxinogenic bacteria isolated

SIR,—Dr T Wadström and his colleagues (5 June, p 1401) reported the isolation of enterotoxinogenic *Escherichia coli* from 28 out of 640 patients with diarrhoea in Sweden and observed that 24 of these 28 had been abroad during the two weeks before sampling. Studies in the USA¹ have shown enterotoxinogenic *E coli* to be an important cause of diarrhoea in travellers to Mexico. We have recently completed a small survey of patients admitted to hospital in the United Kingdom with persistent diarrhoea which first developed during travel in Africa and Asia.

Sixteen adult patients were included in the survey. Faecal specimens obtained shortly after admission to hospital were examined by direct microscopy for the presence of ova and cysts and by routine methods for salmonellae, shigellae, and vibrios. In addition five representative colonies selected from MacConkey agar cultures were identified biochemically and

those identified as *E coli* were serotyped using antisera for somatic antigens O1–O163 and flagella antigens H1–H56. A representative culture of each serotype found in each patient was tested for enterotoxin production. One representative culture of any other species of Enterobacteriaceae from each patient was similarly tested. The infant mouse test² was used for the detection of heat-stable enterotoxin (ST) and the CHO cell³ and Y1 cell⁴ tests were used to detect heat-labile enterotoxin (LT).

Five patients had *Giardia lamblia* in their stools and one patient was excreting cysts of *Entamoeba histolytica*. Salmonellae, shigellae, and vibrios were not found. Only 12 patients were found to be excreting *E coli*; in two patients only Gram-positive organisms were found, one patient excreted only *Citrobacter freundii* and one excreted a mixture of *C freundii*, *Hafnia alvei*, and *Enterobacter* sp. A total of 28 *E coli* and seven other organisms were tested for enterotoxin production; these included 2 *C freundii*, 2 *Enterobacter* sp, 1 *Proteus* sp, 1 *Klebsiella* sp, and 1 *Hafnia alvei*. None of the organisms produced ST, but LT production was demonstrated in *E coli* from two patients who had travelled overland to Nepal. In both patients the serotype was O114 H49.

These results support the possible role of enterotoxinogenic *E coli* as a cause of diarrhoea in adults. The study in the USA¹ was concerned with acute diarrhoea developing shortly after arrival in Mexico. The present study suggests that enterotoxinogenic *E coli* may also be implicated in diarrhoea which developed overseas but persisted for up to six weeks. Further studies are required and we would be pleased to receive cultures of *E coli* isolated from patients returning to the UK with diarrhoea which developed while they were abroad or who develop diarrhoea within a few days of returning to the UK. Such strains should be sent to Dr B Rowe at the address given below.

We acknowledge the assistance of Dr R Grüneberg and the staff of the Bacteriology Department, University College Hospital, London.

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¹ Sack, D A, et al, *Lancet*, 1975, 2, 239.

² Dean, A G, et al, *Journal of Infectious Diseases*, 1972, 125, 407.

³ Guerrant, R L, et al, *Infection and Immunity*, 1974, 10, 320.

⁴ Donta, S T, Moon, H W, and Whipp, S C, *Science*, 1974, 183, 334.

Glutethimide and enzyme induction

SIR,—We would agree with Drs J A Mathews and D A H Yates (23 October, p 1014) that the enzyme-inducing properties of glutethimide should be more widely appreciated. Glutethimide has been shown to shorten warfarin plasma half lives,¹ to decrease steady-state plasma warfarin levels,² and thus to decrease the hypoprothrombinaemic effect of warfarin.³

A recent pilot study of enzyme induction in man has provided information on the time course of this effect. Three healthy male